CLAIMS

1. An isolated polynucleotide having a nucleic acid sequence which is capable of ~~hybridising~~ under high stringency conditions with the polynucleotide sequence ~~presented as~~ SEQ ID NO: 1, its complementary strand, or a sub-sequence thereof.

2. The isolated polynucleotide according to claim 1, being at least 50% homologous, preferably more than 70%, more preferred more than 80%, even more preferred more than 90%, most preferred more than 95%, homologous to the polynucleotide sequence presented as SEQ ID NO: 1.

3. The isolated polynucleotide according to either of claims 1-2 being a cloned polynucleotide.

4. The isolated polynucleotide according to claim 3, in which the polynucleotide is cloned from, or produced on the basis of a cDNA library.

5. The isolated polynucleotide according to ~~any of claims 1-4~~, comprising the polynucleotide sequence ~~presented as~~ SEQ ID NO: 1, or a sub-sequence ~~hereof~~.

6. The isolated polynucleotide according to any of claims 1-4, comprising the polynucleotide sequence presented as SEQ ID NO: 1, or a sub-sequence hereof, including the mutation G935A.

7. The isolated polynucleotide according to any of claims 1-6, encoding a potassium channel, or a potassium channel subunit.

8. The isolated polynucleotide according to claim 7, encoding ~~the~~ KCNQ4 potassium channel subunit comprising the amino acid sequence ~~represented by~~ SEQ ID NO: 2, or a sub-sequence ~~hereof~~.

9. The isolated polynucleotide according to claim 7, encoding a KCNQ4 variant, ~~which~~ variant has an amino acid sequence that has been changed by deletion of an amino acid residue, by insertion of an additional amino acid residue, or by substitution of an amino acid residue at one or more positions.

10. The isolated polynucleotide according to claim 9, which variant has an amino acid sequence that has been changed at one or more positions located in the conserved regions, as defined by Table 1.

11. The isolated polynucleotide according to claim 9, encoding the variant KCNQ4/G285S (i.e. KCNQ4/G333S according to the KCNQ1 numbering).

12. An isolated polynucleotide comprising any one of the sequences ~~set forth in~~ SEQ ID NOS: 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, and 32.

13. A recombinantly produced polypeptide encoded by the polynucleotide according to claims ~~1-11~~.

14. The polypeptide according to claim 13, being a KCNQ4 potassium channel subunit comprising the amino acid sequence presented as SEQ ID No. 2.

15. The polypeptide according to claim 13, being a KCNQ4 variant, which variant has an amino acid sequence that has been changed by deletion of an amino acid residue, by insertion of an additional amino acid residue, or by substitution of an amino acid residue at one or more positions.

16. The polypeptide according to claim 15, which variant has an amino acid sequence that has been changed at one or more positions located in the conserved regions, as defined by Table 1.

17. The polypeptide according to claim 15, being the variant KCNQ4/G285S (i.e. KCNQ4/G333S according to the KCNQ1 numbering).

18. A cell genetically manipulated by the incorporation of a heterologous polynucleotide according to ~~any of claims 1-11~~.

19. The cell according to claim 18, genetically manipulated by the incorporation of a KCNQ4 channel subunit comprising the amino acid sequence ~~presented as~~ SEQ ID NO: 2, or a sub-sequence hereof.

20. The cell according to claim 18, genetically manipulated by the incorporation of a KCNQ4 variant, ~~which~~ variant has an amino acid sequence that has been

changed by deletion of an amino acid residue, by insertion of an additional amino acid residue, or by substitution of an amino acid residue at one or more positions.

21. The cell according to claim 20, which variant has an amino acid sequence that has been changed at one or more positions located in the conserved regions, as defined by Table 1.

22. The cell according to claim 20, genetically manipulated by the incorporation of the variant KCNQ4/G285S (i.e. KCNQ4/G333S according to the KCNQ1 numbering).

23. The cell according to any of claims 18-22, genetically manipulated to co-express one or more KCNQ channel subunits.

24. The cell according to claim 23, genetically manipulated to co-express KCNQ4 and KCNQ1 channel subunits; KCNQ4 and KCNQ2 channel subunits; KCNQ4 and KCNQ3 channel subunits; KCNQ4 and KCNQ1 and KCNQ2 channel subunits; KCNQ4 and KCNQ1 and KCNQ3 channel subunits; KCNQ4 and KCNQ2 and KCNQ3 channel subunits; or KCNQ4 and KCNQ1 and KCNQ2 and KCNQ3 channel subunits.

25. The cell according to claim 23, genetically manipulated to co-express KCNQ3 and KCNQ4 channel subunits.

26. The cell according to any of claims 18-25, being an eukaryotic cell, in particular a mammalian cell, an oocyte, or a yeast cell.

27. The cell according to any claim 26, being a human embryonic kidney (HEK) cell, a HEK 293 cell, a BHK21 cell, a Chinese hamster ovary (CHO) cell, a *Xenopus laevis* oocyte (XLO) cell, a COS cell, or any other cell line able to express KCNQ potassium channels.

28. A membrane preparation derived from a cell according to ~~any of claims 18-27~~.

29. A method for obtaining a substantially homogeneous source of a human potassium channel, comprising a KCNQ4 subunit, which method comprises the steps of culturing a cellular host having incorporated expressibly therein a

polynucleotide according to any of claims 1-11, and then recovering the cultured cells.

30. The method of claim 29, comprising the ~~subsequent~~ step of obtaining a membrane preparation from the cultured cells.

31. A method of screening a chemical compound for capability of binding to a potassium channel comprising at least one KCNQ4 channel subunit, which method comprises the steps of

(i) subjecting a KCNQ4 channel subunit containing cell according to claims 18-27, or a membrane preparation according to claim 28, to the action of a KCNQ4 binding agent to form a complex with the KCNQ4 channel subunit containing cell;

(ii) subjecting the complex of step (i) to the action of the chemical compound to be tested; and

(iii) detecting the displacement of the KCNQ4 binding agent from the complex with the KCNQ4 channel subunit containing cell or membrane preparation.

32. The method of claim 31, wherein the KCNQ4 channel subunit containing cell is a cell according to any of claims 18-27, or a membrane preparation according to claim 28.

33. The method of ~~either of claims 31-32, in which~~ the KCNQ4 binding agent is

radioactively labelled 1,3-dihydro-1-phenyl-3,3-bis(4-pyridylmethyl)-2H-indol-2-one (~~Linopirdine~~); or

radioactively labelled 10,10-bis(4-pyridinyl-methyl)-9(10H)-antracenone.

34. The method of claim 33, which compounds have been marked with ^{3}H.

35. The method of ~~either of claims 33-34~~, wherein the displacement of the KCNQ4 binding agent from the complex with the KCNQ4 channel subunit ~~containing~~ cell is detected by measuring ~~the~~ amount of radioactivity by conventional liquid scintillation counting.

36. A method of screening a chemical compound for activity on a potassium channel comprising at least one KCNQ4 channel subunit, which method comprises the steps of

(i) subjecting a KCNQ4 channel subunit containing cell to the action of the chemical compound; and

(ii) monitoring the membrane potential, the current, the potassium flux, or the secondary calcium influx of the KCNQ4 channel subunit containing cell.

37. The method of claim 36, wherein ~~the KCNQ4 channel subunit containing~~ cell is a cell according to ~~any of claims 18-27~~.

38. The method of ~~either of claims 36-37~~, wherein monitoring of the membrane potential ~~of the KCNQ4 channel~~ subunit ~~containing cell~~ is performed by patch clamp techniques.

39. The method of ~~either of claims 36-37~~, wherein monitoring of the membrane potential ~~of the KCNQ4 channel subunit containing cell~~ is performed ~~using~~ fluorescence methods.

40. A chemical compound identified by the method of ~~claims 31-35, and/or by the method of claims 36-39~~.

41. Use of the chemical compound according to claim 40 for diagnosis, treatment, prevention or alleviation of diseases related to tinnitus, loss of hearing, in particular progressive hearing loss, neonatal deafness, and presbyacusis (deafness of the elderly); and diseases or adverse conditions of the CNS, including affective disorders, Alzheimer's disease, anxiety, ataxia, CNS damage caused by trauma, stroke or neurodegenerative illness, cognitive deficits, compulsive behaviour, dementia, depression, Huntington's disease, mania, memory impairment, memory disorders, memory dysfunction, motion disorders, motor disorders, neurodegenerative diseases, Parkinson's disease and Parkinson-like motor disorders, phobias, Pick's disease, psychosis, schizophrenia, spinal cord damage, stroke, and tremor.

42. The ~~use~~ according to claim 41, wherein the chemical compound is 1,3-dihydro-1-phenyl-3,3-bis(4-pyridylmethyl)-2H-indol-2-one (~~Linopirdine~~); or
10,10-bis(4-pyridinyl-methyl)-9(10H)-antracenone.

43. Use of a polynucleotide sequence according to any of claims 1-12, for the screening of genetic materials for individuals having this mutations.

44. A transgenic animal comprising a knock-out mutation of the endogenous *KCNQ4* ~~gene, a~~ mutated *KCNQ4* ~~gene, or genetically manipulated in order to over-express the *KCNQ4* gene or to over-express mutated *KCNQ4* gene~~.

45. The transgenic animal according to claim 44, being a knock-out animal in which the gene is totally deleted in a homozygous state.

46. The transgenic animal according to claim 44, comprising a mutated *KCNQ4* gene.

47. The transgenic animal according to any of claims 44-46, being a transgenic rodent, in particular a hamster, a guinea pig, a rabbit, or a rat, a transgenic pig, a transgenic cattle, a transgenic sheep, or a transgenic goat.

48. Use of the transgenic animal according to any of claims 44-47 for the *in vivo* screening of therapeutic compounds.

49. The use according to claim 48, for the screening of drugs affecting diseases or conditions associated with hearing loss or tinnitus.

50. A method for the identification, localization, isolation or amplification a polynucleotide according to any one of claims 1-11, comprising using a polynucleotide according to claim 12 as a primer or a probe.

51. An antibody capable of binding one or more polypeptides as claimed in any one of claims 13-17.

52. The antibody of claim 51 being a monoclonal antibody.